```
=> d his

     (FILE 'HOME' ENTERED AT 13:30:24 ON 12 SEP 2005)

     FILE 'CAPLUS' ENTERED AT 13:30:35 ON 12 SEP 2005
L1             1 S US6645950/PN
               SELECT L1 1 RN
L2         11712 S E1-E35

     FILE 'REGISTRY' ENTERED AT 13:31:38 ON 12 SEP 2005
L3             1 S 209803-68-9/RN
               SET NOTICE 1 DISPLAY
               SET NOTICE LOGIN DISPLAY

     FILE 'REGISTRY' ENTERED AT 13:31:56 ON 12 SEP 2005
L4             1 S 15761-38-3/RN
               SET NOTICE 1 DISPLAY
               SET NOTICE LOGIN DISPLAY

     FILE 'REGISTRY' ENTERED AT 13:32:13 ON 12 SEP 2005
L5             1 S 29178-60-7/RN
               SET NOTICE 1 DISPLAY
               SET NOTICE LOGIN DISPLAY

     FILE 'REGISTRY' ENTERED AT 13:32:45 ON 12 SEP 2005
L6             1 S 56073-91-7/RN
               SET NOTICE 1 DISPLAY
               SET NOTICE LOGIN DISPLAY

     FILE 'REGISTRY' ENTERED AT 13:35:29 ON 12 SEP 2005
L7             1 S 34840-23-8/RN
               SET NOTICE 1 DISPLAY
               SET NOTICE LOGIN DISPLAY

     FILE 'REGISTRY' ENTERED AT 13:35:55 ON 12 SEP 2005
L8             1 S 56073-96-2/RN
               SET NOTICE 1 DISPLAY
               SET NOTICE LOGIN DISPLAY

     FILE 'REGISTRY' ENTERED AT 13:36:42 ON 12 SEP 2005
L9             1 S 72447-64-4/RN
               SET NOTICE 1 DISPLAY
               SET NOTICE LOGIN DISPLAY

     FILE 'REGISTRY' ENTERED AT 13:40:24 ON 12 SEP 2005
L10            1 S 93958-45-3/RN
               SET NOTICE 1 DISPLAY
               SET NOTICE LOGIN DISPLAY
L11           29 S E4-E26, E29-E34

     FILE 'CAPLUS' ENTERED AT 13:42:06 ON 12 SEP 2005
L12           43 S L11
L13            1 S L12 AND (CANCER? OR TUMOR? OR NEOPLAST? OR CARCINO?)

     FILE 'USPATFULL, USPAT2' ENTERED AT 13:47:35 ON 12 SEP 2005
L14            4 S L12
L15            3 S L14 AND (CANCER? OR TUMOR? OR NEOPLAST? OR CARCINO?)

     FILE 'CAPLUS' ENTERED AT 13:57:47 ON 12 SEP 2005
L16            1 S L12  AND (CANCER? OR TUMOR? OR NEOPLAST? OR CARCINO? OR PROLI

     FILE 'REGISTRY' ENTERED AT 14:00:11 ON 12 SEP 2005
L17            1 S 56073-98-4/RN
               SET NOTICE 1 DISPLAY
               SET NOTICE LOGIN DISPLAY

     FILE 'EPFULL, FRFULL, GBFULL, PATDPAFULL, PCTFULL, RDISCLOSURE,
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L18           3 S L16

     FILE 'MEDLINE' ENTERED AT 14:08:53 ON 12 SEP 2005
L19           0 S L18
L20           0 S L12 AND (CANCER? OR TUMOR? OR NEOPLAST? OR CARCINO? OR PROLIF

     FILE 'CAPLUS' ENTERED AT 14:12:32 ON 12 SEP 2005
L21           2 S L20

     FILE 'USPATFULL, USPAT2' ENTERED AT 14:13:09 ON 12 SEP 2005
L22           3 S L20

     FILE 'MEDLINE' ENTERED AT 14:15:45 ON 12 SEP 2005
L23         408 S (HELMINTH? OR ANTHELMINT?)(L)(CANCER? OR TUMOR? OR NEOPLAST?
L24         225 S L23 NOT PY>=1999
L25         173 S (HELMINTH? OR ANTHELMINT?)(L)(CANCER? OR TUMOR? OR NEOPLAST?
L26          92 S L25 NOT PY>=1999

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L1             1 US6645950/PN

=> select l1
ENTER ANSWER NUMBER OR RANGE (1-):1
ENTER DISPLAY CODE (TI) OR ?:rn
E1 THROUGH E35 ASSIGNED

=> s e1-e35
          8785 103-71-9/BI
            89 117924-33-1/BI
          2663 15761-38-3/BI
             3 209803-68-9/BI
             1 284019-29-0/BI
             1 284019-30-3/BI
             1 284019-31-4/BI
             1 284019-34-7/BI
             1 284019-36-9/BI
             1 284019-39-2/BI
             1 284019-41-6/BI
             1 284019-43-8/BI
             1 284019-44-9/BI
             1 284019-46-1/BI
             1 284019-47-2/BI
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             1 284019-58-5/BI
             1 284019-59-6/BI
             5 29178-60-7/BI
           175 34840-23-8/BI
             5 56073-91-7/BI
             6 56073-92-8/BI
             5 56073-95-1/BI
            13 56073-96-2/BI
             4 56073-98-4/BI
            27 72447-64-4/BI
             2 93958-45-3/BI
L2         11712 (103-71-9/BI OR 117924-33-1/BI OR 15761-38-3/BI OR 209803-68-9/B
                 I OR 284019-29-0/BI OR 284019-30-3/BI OR 284019-31-4/BI OR 28401
                 9-34-7/BI OR 284019-36-9/BI OR 284019-39-2/BI OR 284019-41-6/BI
                 OR 284019-43-8/BI OR 284019-44-9/BI OR 284019-46-1/BI OR 284019-
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                 OR 284019-51-8/BI OR 284019-52-9/BI OR 284019-53-0/BI OR 284019-
                 55-2/BI OR 284019-56-3/BI OR 284019-57-4/BI OR 284019-58-5/BI
                 OR 284019-59-6/BI OR 29178-60-7/BI OR 34840-23-8/BI OR 56073-91-
                 7/BI OR 56073-92-8/BI OR 56073-95-1/BI OR 56073-96-2/BI OR 56073
                 -98-4/BI OR 72447-64-4/BI OR 93958-45-3/BI)
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e4

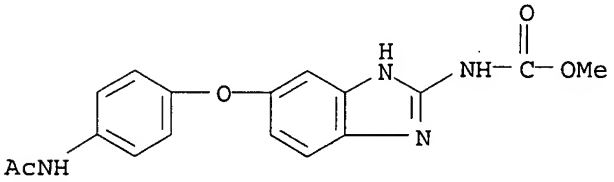
e26

e29

e34

(e4-e26
(e29-e34

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN **56073-91-7** REGISTRY
CN Carbamic acid, [5-[4-(acetylamino)phenoxy]-1H-benzimidazol-2-yl]-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C17 H16 N4 O4
LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

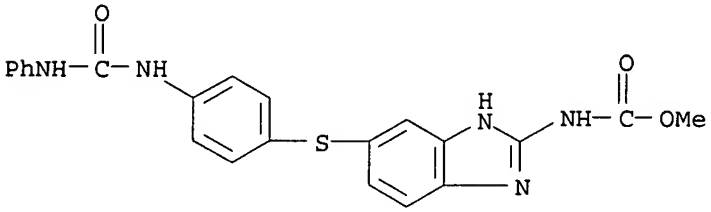


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

Instant Compound

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN **209803-68-9** REGISTRY
CN Carbamic acid, [5-[[4-[[(phenylamino)carbonyl]amino]phenyl]thio]-1H-benzimidazol-2-yl]-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H19 N5 O3 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent)

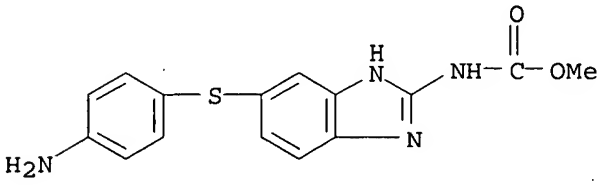


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

instant Compound

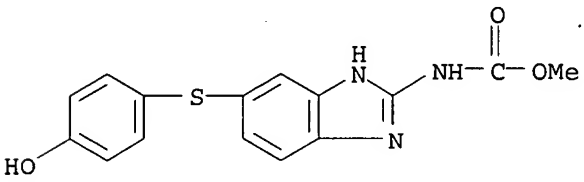
L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN **56073-96-2** REGISTRY
CN Carbamic acid, [5-[(4-aminophenyl)thio]-1H-benzimidazol-2-yl]-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C15 H14 N4 O2 S
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

13 REFERENCES IN FILE CA (1907 TO DATE)
13 REFERENCES IN FILE CAPLUS (1907 TO DATE)

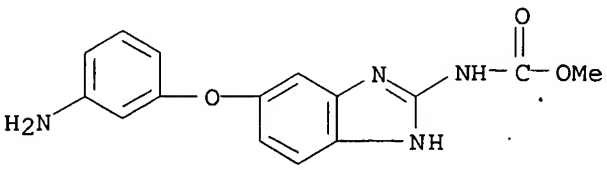
L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN **72447-64-4** REGISTRY
CN Carbamic acid, [5-[(4-hydroxyphenyl)thio]-1H-benzimidazol-2-yl]-, methyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN HOE 2542
CN p-Hydroxyfenbendazole
FS 3D CONCORD
MF C15 H13 N3 O3 S
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, DDFU, DRUGU, MEDLINE, TOXCENTER, USPATFULL, VETU
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process); PRP (Properties); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

27 REFERENCES IN FILE CA (1907 TO DATE)
27 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L17 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN **56073-98-4** REGISTRY
CN Carbamic acid, [5-(3-aminophenoxy)-1H-benzimidazol-2-yl]-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C15 H14 N4 O3
LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PROC (Process)



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4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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L15 ANSWER 1 OF 3 USPATFULL on STN
ACCESSION NUMBER: 2004:108181 USPATFULL
TITLE: Chemical compounds
INVENTOR(S): Cheung, Mui, Durham, NC, UNITED STATES
Harris, Philip Anthony, Durham, NC, UNITED STATES
Hasegawa, Masaichi, Tsukuba-shi, JAPAN
Ida, Satoru, Keita, JAPAN
Kano, Kazuya, Tsukuba-shi, JAPAN
Nishigaki, Naohiko, Tsukuba-shi, JAPAN
Sato, Hideyuki, Tsukuba-shi, JAPAN
Veal, James Marvin, Apex, NC, UNITED STATES
Washio, Yoshiaki, Tsukuba-shi, JAPAN
West, Rob I., Stevenage, UNITED KINGDOM

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004082583	A1	20040429	
APPLICATION INFO.:	US 2003-433128	A1	20031112	(10)
	WO 2001-US44553		20011128	

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: DAVID J LEVY, CORPORATE INTELLECTUAL PROPERTY, GLAXOSMITHKLINE, FIVE MOORE DR., PO BOX 13398, RESEARCH TRIANGLE PARK, NC, 27709-3398
NUMBER OF CLAIMS: 95
EXEMPLARY CLAIM: 1
LINE COUNT: 5806
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 2 OF 3 USPATFULL on STN
ACCESSION NUMBER: 2004:77193 USPATFULL
TITLE: Benzimidazole vascular damaging agents
INVENTOR(S): Davis, Peter David, Watlington, UNITED KINGDOM

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004058972	A1	20040325	
APPLICATION INFO.:	US 2003-612163	A1	20030703	(10)

instant application

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-889061, filed on 22 Oct 2001, GRANTED, Pat. No. US 6645950

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1999-752	19990115
	WO 2000-GB99	20000114

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PATENT ADMINSTRATOR, KATTEN MUCHIN ZAVIS ROSENMAN, 525 WEST MONROE STREET, SUITE 1600, CHICAGO, IL, 60661-3693
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
LINE COUNT: 774
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 3 OF 3 USPATFULL on STN
ACCESSION NUMBER: 2003:296918 USPATFULL
TITLE: Benzimidazole vascular damaging agents
INVENTOR(S): Davis, Peter David, Watlington, UNITED KINGDOM
PATENT ASSIGNEE(S): Angiogene Pharmaceuticals Ltd., Oxfordshire, UNITED KINGDOM (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6645950	B1	20031111
	WO 2000041669		20000720

parent Case

APPLICATION INFO.:	US 2001-889061	20011022 (9)
	WO 2000-GB99	20000114

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1999-752	19990115

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Stockton, Laura L.
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 731
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:295616 CAPLUS
DOCUMENT NUMBER: 122:95971
TITLE: Benzimidazoles, potent anti-mitotic drugs: substrates for the P-glycoprotein transporter in multidrug-resistant cells
AUTHOR(S): Nare, Bakela; Liu, Zhi; Prichard, Roger K.; Georges, Elias
CORPORATE SOURCE: Inst. Parasitology, McGill Univ., Anne de Bellevue, QC, H9X 3V9, Can.
SOURCE: Biochemical Pharmacology (1994), 48(12), 2215-22
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB P-glycoprotein is thought to mediate the energy-dependent efflux of many structurally and functionally unrelated lipophilic compds. Presently, the mol. mechanism underlying the binding and efflux of drugs by P-glycoprotein is not well understood. However, it has been suggested that two planar benzene ring structures and a cationic charge are commonly found in many drugs that interact with P-glycoprotein. The benzimidazoles (BZs) are potent anti-**tumor**, anti-fungal and anti-parasitic agents, whose mode of action is thought to result from their inhibition of microtubule functions. Although other classes of microtubule inhibitors, such as colchicine and vinblastine, have been studied extensively with respect to their interaction and efflux by P-glycoprotein, the BZ group of drugs has not been characterized. In this study, the authors have characterized the interaction of BZ with multidrug-resistant cells and found that resistant cells accumulated substantially less BZ compared with drug-sensitive cells. Furthermore, BZ was more toxic to sensitive than to drug-resistant cells, suggesting that BZ is likely to be a substrate for the P-glycoprotein drug efflux pump. In addition, the authors used a photoactive analog of BZ ([125I]ASA-BZ) to demonstrate a direct binding between BZ and P-glycoprotein. Results showing that a molar excess of vinblastine, unmodified BZ, verapamil and rhodamine 123, but not colchicine, inhibited the photoaffinity labeling of P-glycoprotein by [125I]ASA-BZ confirmed the binding specificity of BZ to P-glycoprotein. Protease digestion of [125I]ASA-BZ photoaffinity labeled P-glycoprotein yielded two peptides that were similar to those obtained with other P-glycoprotein-associated drugs, e.g., azidopine and iodoaryl azidoprazosin. Taken together, these results demonstrate a direct and specific interaction between P-glycoprotein and BZ in a manner that is probably similar to other previously characterized P-glycoprotein-associated drugs.
AB P-glycoprotein is thought to mediate the energy-dependent efflux of many structurally and functionally unrelated lipophilic compds. Presently, the mol. mechanism underlying the binding and efflux of drugs by P-glycoprotein is not well understood. However, it has been suggested that two planar benzene ring structures and a cationic charge are commonly found in many drugs that interact with P-glycoprotein. The benzimidazoles (BZs) are potent anti-**tumor**, anti-fungal and anti-parasitic agents, whose mode of action is thought to result from their inhibition of microtubule functions. Although other classes of microtubule inhibitors, such as colchicine and vinblastine, have been studied extensively with respect to their interaction and efflux by P-glycoprotein, the BZ group of drugs has not been characterized. In this study, the authors have characterized the interaction of BZ with multidrug-resistant cells and found that resistant cells accumulated substantially less BZ compared with drug-sensitive cells. Furthermore, BZ was more toxic to sensitive than to drug-resistant cells, suggesting that BZ is likely to be a substrate for the P-glycoprotein drug efflux pump. In addition, the authors used a photoactive analog of BZ ([125I]ASA-BZ) to demonstrate a direct binding between BZ and P-glycoprotein. Results showing that a molar excess of vinblastine, unmodified BZ, verapamil and rhodamine 123, but not colchicine, inhibited the photoaffinity labeling of P-glycoprotein by [125I]ASA-BZ confirmed the binding specificity of BZ to P-glycoprotein. Protease digestion of [125I]ASA-BZ photoaffinity labeled P-glycoprotein yielded two peptides that were similar to those obtained with other P-glycoprotein-associated drugs, e.g., azidopine and iodoaryl azidoprazosin.

Taken together, these results demonstrate a direct and specific interaction between P-glycoprotein and BZ in a manner that is probably similar to other previously characterized P-glycoprotein-associated drugs.

IT **56073-98-4**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(benzimidazoles as potent anti-mitotic drugs and substrates for P-glycoprotein transporter in multidrug-resistant cells)